

Remarks

Claims 1-13 were pending in the subject application. By this Amendment, claims 1, 2, 5, 6, 8, 11, and 13 have been amended, claims 3, 7, 9 and 10 have been cancelled, and new claim 16 has been added. The undersigned avers that no new matter is introduced by this Amendment. Support for the new claims and amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Claims 8, and 11-13 remain pending but withdrawn from consideration. Accordingly, claims 1, 2, 4-6, and 16 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Applicants acknowledge that claims 8 and 11-13 have been withdrawn from further consideration as being drawn to a non-elected invention. However, Applicants wish to reserve the right to rejoinder of the non-elected method claims upon an indication of an allowable product claim in accordance with MPEP §821.04.

By this Amendment, claims 1, 2, 5, 6, 8, 11, and 13 have been amended, and claim 16 has been added. Support for the amendments to claims 1, 6, 8, 11, and 13, and for claim 16 can be found in the application at page 4, lines 30-32; page 7, lines 1-17; and the claims as originally filed. Claims 2 and 5 were amended for informalities.

The Examiner has objected to the drawings for containing reference characters that are not referenced in the Brief Description of the Drawings (namely, A and B of Figure 7). Applicants have amended the subject specification to include a brief description of the cited figures as suggested by the Examiner. Support for this amendment can be found, for example, in Example 5, at page 11 of the specification. Reconsideration and withdrawal of the objection is respectfully requested.

The Examiner has objected to claims 2 and 5 for informalities. By this Amendment, claims 2 and 5 have been amended to replace the terms “EGF”, “FGF-2”, and “TGF β ” with “epidermal growth factor”, “fibroblast growth factor-2”, and “transforming growth factor β ”, respectively. In addition, a comma has been inserted in claim 5 between fibroblast growth factor-2 and retinoic acid. Accordingly, reconsideration and withdrawal of the objections to the claims is respectfully requested.

Claim 6 is rejected under 35 USC §102(b) as anticipated by Fischer *et al.* (*Glia*, 2003, 43:70-76). Applicants respectfully submit that the Fischer *et al.* publication does not anticipate the claimed composition. However, in order to expedite prosecution of the subject application, Applicants have amended claim 6 to recite that the composition comprises dedifferentiated Müller cells obtainable by culturing human adult Müller cells in the presence of an extracellular matrix protein and a growth factor to thereby induce dedifferentiation of the Müller cells. In contrast, the Fischer *et al.* publication discloses studies into dedifferentiation of Müller cells *in vivo* in the neonatal chick retina in the presence of growth factors.

As the Examiner is aware, to be anticipatory under 35 U.S.C. §102(b), a single prior art reference must disclose each and every element as set forth in the claim, either expressly or inherently. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631; 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). As the Fischer *et al.* publication does not disclose the dedifferentiated Müller cells obtained by the steps recited in the claim, Applicants respectfully submit that the Fischer *et al.* reference does not anticipate the claimed invention. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §102(b) is respectfully requested.

Claims 1-7 are rejected under 35 USC §103(a) as obvious over Keating *et al.* (U.S. Patent Publication No. 2004/0087016) in view of Fischer *et al.* (*Glia*, 2003, 43:70-76). Applicants respectfully traverse this ground for rejection and assert that the claimed invention is not obvious over the cited references.

By this Amendment, independent claims 1 and 6 have been amended to recite that the dedifferentiated Müller cells are human cells. The Keating *et al.* publication is based upon experiments carried out in the newt. It has been recognized since the 1960s that fish and amphibians are able to regenerate tissues throughout life, allowing them to grow new limbs and retina spontaneously after injury. However, these properties have not been clearly identified in mammals, especially humans, as is indicated in paragraph [0003] on page 1 of the Keating *et al.* publication, which states that “Echinoderms and crustaceans are likewise capable of regeneration. However, with the exception of liver, mammals, such as humans, lack this remarkable regenerative capability.”

Although the Keating *et al.* publication refers to the potential of various cell sources that may be capable of regenerating organs, there are no specific examples of dedifferentiating any of the cell

types and, indeed, Müller stem cells are not mentioned. Therefore, from the Keating *et al.* publication, it would not have been obvious to those of ordinary skill in the art that Müller stem cells could be isolated from the adult human retina to generate neurons. It is asserted in the Office Action that it would have been obvious to combine the teachings of Fischer *et al.*, which is directed to dedifferentiation of Müller cells, with the Keating *et al.* publication in order to arrive at the claimed invention. However, as discussed above in response to the rejection under 35 U.S.C. §102(b), the Fischer *et al.* publication discloses *in vivo* studies into dedifferentiation of Müller glia in the neonate avian retina. As described on page 76, second paragraph, the authors of the Fischer *et al.* publication did not find evidence of such cells in the adult avian retina and suggested that “the postnatal chicken retina may suppress the differentiation of the Müller glia-derived progenitors.” This statement clearly indicates that there was no obvious presence of Müller stem cell function in the adult avian retina. Based upon this teaching, there would be no reason for one of ordinary skill in the art to expect that the adult human retina would contain such cells. In fact, the disclosure in this publication would actually direct one of ordinary skill in the art away from the currently claimed invention. A prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); MPEP §2141.02 (V).

Furthermore, the authors of the Fischer *et al.* publication did not attempt to isolate the cells from the avian retina or to culture these cells *in vitro*. All the work in the Fischer *et al.* publication was performed *in situ* by injecting neurotoxins and growth factors into the neonate avian retina. In contrast, as demonstrated within the subject specification, the inventors have isolated these cells from the adult human retina and have grown and maintained them *in vitro*. This is not known or taught by the cited references, and the cited references confer no reasonable expectation of success in doing so. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. MPEP §2143.01. Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976); MPEP §2143.02.

For the foregoing reasons, Applicants respectfully assert that the claimed invention is not obvious over the cited references. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Glenn P. Ladwig
Patent Attorney
Registration No. 46,853
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

GPL/jnw